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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,785	04/25/2006	John Nolting	PA1394	2982

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MEDTRONIC VASCULAR, INC.
IP LEGAL DEPARTMENT
3576 UNOCAL PLACE
SANTA ROSA, CA 95403

EXAMINER	
HELM, CARALYNNE E	

ART UNIT	PAPER NUMBER
1615	

NOTIFICATION DATE	DELIVERY MODE
10/30/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

rs.vasciplegal@medtronic.com

Office Action Summary	Application No.	Applicant(s)	
	10/563,785	NOLTING, JOHN	
	Examiner	Art Unit	
	CARALYNNE HELM	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,7-12,14,15 and 18-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 7-12, 14-15, and 18-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 20, 2009 has been entered.

MAINTAINED REJECTIONS

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The four factual inquiries of Graham v. John Deere Co. have been fully considered and analyzed in the rejections that follow.

Claims 12-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. (US PGPub No. 2003/0153983).

Miller et al, teach medical devices with a set of layers on their surface that can each contain a different bioactive (see abstract and paragraph 55; instant claim 12). In particular, Miller et al. envision coronary stents as medical devices within their invention (see paragraph 92; instant claim 12). One of ordinary skill in the art at the time of the invention would have found it obvious to select a particular set of therapeutic agents pertinent to the body region treated by the device (e.g. coronary artery). Therapeutic agents considered by Miller et al. are taught to include paclitaxel, dexamethasone, and non-steroidal anti-inflammatory agents (see paragraphs 45 and 49; instant claims 14-15). These therapeutic containing layers are also taught to be composed of biodegradable (bioerodable) polymers (see paragraphs 40-41; instant claim 13). Miller et al. also teach that the layers are applied to any portion of the device, thus it also would have been obvious to apply them to the full length of the device (which includes the distal, proximal, and mid-portions) (see paragraph 50; instant claims 12 and 19-20). The layered configuration contains a plurality of barrier layers (timing coatings) and a plurality of therapeutic agent containing layers that alternate on the surface of the device (see paragraph 62; instant claim 16). These layers are taught to impede the release of therapeutic agents from the device (see paragraph 56; instant claim 18).

Embodiments are envisioned where a barrier layer (timing coating) covers each of three therapeutic agent containing layers (see paragraph 62; instant claims 12 and 20). The rate of release of drug from this series of layers increases as their distance from the surface decreases. Therefore this embodiment embraces sequential delivery of drugs for at least an initial time period (e.g. the outermost drug releases first, followed by the drug in the next layer, followed by the drug in the layer nearest the stent surface; instant claim 12). The barrier layers (timing coatings) are also taught to be composed of biodegradable polymer and in these instances degradation of the layers controls release of the drug (see paragraphs 32 and 58; instant claims 7 and 12). In view of these teachings, it would have been obvious to one of ordinary skill in the art at the time of the invention to employ bioerodable polymers in the barrier layers and the therapeutic containing layers of Miller et al.

Therefore claims 12, 14-15, and 18-20 are obvious over Miller et al.

NEW REJECTIONS

Claim Rejections - 35 USC § 103

Claims 1-3, 7-12, and 19-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. as applied to claims 12 and 14-20 above, and further in view of Sirhan et al. (US PGPub No 2003/0033007 – see IDS - referred to henceforth as Sirhan et al reference B) and as evidenced by Fischell et al. (US PGPub No. 0002755).

Miller et al. make obvious a coronary stent with alternating barrier layers (timing coating) and therapeutic containing layers that all contain bioerodable polymers and are

arranged such that the distal and proximal ends have a plurality of each while the mid-portion has at least one of each. In addition, the claimed therapeutic agents, release kinetics and presence of bioerodable polymers in each layer are also made obvious over Miller et al. (see instant claims 1-3, 7-9, and 24-25). Miller et al. do not teach that the coronary stent is operably coupled to a catheter or that the therapeutic on the mid-region is different than that on the distal and proximal ends.

Sirhan et al. reference B teaches that an edge effect phenomenon is known to occur in patients that have had coronary stents deployed within them (see paragraph 19). Beyond the edges of the implanted stent severe stenosis often develops, thus the inventors developed a device that focuses drug delivery from the proximal and distal ends of a stent device that extends beyond the ends of the stent (see paragraph 22). The intermediate portion (mid-portion) of the stent between the distal and proximal regions is taught to have a therapeutic agent that is different and released with a different kinetic profile than that released from the ends (see paragraph 51; instant claims 10 and 21). These therapeutic agents are taught to be present in coating form on the stent (see paragraph 59). Particular therapeutic agents envisioned on the device, separately or in combination, include dexamethasone, rapamycin, rapamycin analogs, and prednisone (see paragraph 35; instant claims 3 and 15). Sirhan et al. reference B teaches that the stent is deployed via a balloon catheter (requiring that the stent and catheter be operably coupled) (see paragraph 48; instant claim 1). In addition, the presence of a biodegradable (bioerodable) rate controlling element (layer) that impedes the delivery of drug from the intermediate region (mid-portion) as compared to the ends

to different degrees is also taught (see paragraphs 25 and 33; instant claim 9). Sirhan et al. reference B also teaches that the therapeutic has a higher diffusion rate from the device at the ends than in the intermediate region (mid-portion) (see claim 7; instant claims 11 and 22). Sirhan et al. reference B does not explicitly teach a multi-layered configuration of drug containing coatings.

Since Sirhan et al. reference B and Miller et al. both teach drug eluting stents, it would have been obvious to one of ordinary skill to operably couple the stent of Miller et al. to a catheter so as to facilitate implantation. In addition, it also would have been obvious to configure the coating of Miller et al. in consideration of the stent edge effects as taught by Sirhan et al. reference B. This would yield a stent where the distal and proximal ends have at least two different drug coatings and two barrier (timing) coatings that alternate and can also have the intermediate (mid-region) portion with drug (different from that on the distal and proximal ends) coating and a barrier coating. This triumvirate of drugs would be obvious considering that Miller et al. and Sirhan et al. reference B teach a collection of drugs all known for the same purpose (treating restenosis) and their combination in and subsequent liberation from a stent would have been obvious (see "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) see MPEP 2144.06 and instant claims 8, 10, 26, and 28-29.) From the teachings of Sirhan et al.

reference B, the claimed differences in diffusion characteristics between the distal/proximal regions and intermediate region would follow from the combination of references. Further, since Miller et al. implicitly teach sequential delivery of drugs from their taught layered configuration, sequential delivery of the multiple drugs in the separate layers on the distal and proximal ends would also have been obvious.

Sirhan et al. reference B provides for the deployment of the stent made obvious by their teachings and those of Miller et al. to a vessel. Fischell et al. teach a coated stent where a biodegradable polymer containing barrier layer is on top of a drug layer to control its rate of release (see paragraph 49). They go on to teach that the thickness of the biodegradable is determined by its erosion properties (see paragraph 54). This indicates that the rate of erosion of a biodegradable barrier layer is directly related to the rate of release of the drug from its layer and that such polymer layers are actuated by erosion (see instant claims 1, 23, and 27). Since the polymers in each of the layers are taught to be biodegradable, they would be capable of controlling delivery of drug via erosion. So it then follows that the deployment of the device made obvious by Miller et al. in view of Sirhan et al. that is configured to sequentially deliver the drugs in the distal and proximal ends would do so via the sequential actuation/erosion of overlying layers (e.g. erosion of top barrier allows delivery of first therapeutic; erosion of polymer in first therapeutic layer allows erosion of second barrier layer which then allows delivery of second therapeutic). Furthermore, instant claim 23 contains several active steps that are physiological processes that occur due to the implantation of the claimed stent. No action by man is required or needed after deployment of the device to release the drug,

erode the polymer of the first therapeutic coating, or actuate the first timing coating to release the second therapeutic. While Fischell et al. demonstrate that the delivery mechanism claimed by the instant claims (e.g. instant claims 1 and 23) was known to occur in the claimed degradable barrier layer-drug layer configuration, the claimed structure made obvious by Miller et al. in view of Sirhan et al. reference B would have necessarily functioned in this way upon implantation. Applicant has provided no teachings delineating a subpopulation of particular bioerodable polymers that are necessary to perform in the claimed capacity; therefore, it is the position of the examiner that even in the absence of the teachings of Fischell et al., the release of drug from the stent made obvious by Miller et al. in view of Sirhan et al. reference B would occur via the claimed method upon deployment to a vessel *in vivo*. Thus claims 1-3, 7-12, and 19-29 are obvious over Miller et al. in view of Sirhan et al. reference B and as evidenced by Fischell et al.

Response to Arguments

Applicant's arguments filed July 20, 2009 have been fully considered but they are not persuasive regarding the rejections made under 35 USC 103(a). Arguments regarding maintained rejections are addressed below.

Regarding the rejection under 35 USC 103(a):

Applicant argues that Miller et al. does not teach sequential release of their active agents. Miller et al. teach the use of a configuration of bioactive containing layers alternating with barrier layers such that the compositions of each are modified to control the rate of drug release (see paragraph 62). These barrier layers are taught to be present in part to slow the release of drug contained in the inner most layers. Since it was contemplated to have the drugs deepest in the coating layers release slowest relative to those in the outer most layer, sequential delivery was certainly capable from these devices and follows from the teachings of Miller et al. Given a system where the rate of delivery of two different drugs contained in the same device is different and the slower releasing of the two is placed further from the device surface than the faster releasing drug, there is necessarily a period of time when the drugs are delivered sequentially (e.g. the period before the slow release drug has had enough time to reach the outermost surface). Thus the teachings of Miller et al. do make obvious the sequential delivery of drugs from its series of coatings on a stent device. In addition, applicant does not exclude a period of simultaneous drug delivery from the claimed device nor provide any guidance as to how to produce the claimed stent structure where each layer includes a bioerodable polymer and one drug is not released until after the delivery of another drug has ceased. Further, the barrier coatings of Miller et al. meet the limitations of the claimed timing coating since the only required structure is a bioerodable polymer and applicant has provided no evidence that the biodegradable polymers taught by Miller et al. are not bioerodable. Contrary to applicant's arguments, Miller et al. do not solely teach the delivery of drug from their layered system via

diffusion, but in the case of biodegradable layers, they teach that degradation of the polymer matrix, which includes erosion, also governs drug release (see paragraph 32). Applicant's assertion that Miller does not teach bioerodable polymers in the barrier layer is not supported by the reference, which explicitly envisions biodegradable polymers in these layers (see paragraph 58). Biodegradable polymers are certainly capable of being bioeroded.

Applicant's remaining arguments are moot in light of the new grounds of rejection.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The rejections and/or objections detailed above constitute the complete set presently being applied to the instant application.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CARALYNNE HELM whose telephone number is (571)270-3506. The examiner can normally be reached on Monday through Friday 9-5 (EDT).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Caralynne Helm/
Examiner, Art Unit 1615

/Robert A. Wax/
Supervisory Patent Examiner, Art Unit 1615